The Impact of Agent Orange Exposure on Bladder Cancer
Michael Risk, MD, PhD, Vikram M. Narayan, MD*, Cesar Ercole, MD

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Background & Objectives

- Agent Orange (AO) is a mixture of herbicides used during the Vietnam War to clear forest cover that concealed opposition forces and destroy crops.

- In 2014, the National Academy of Sciences (previously the Institute of Medicine) reported epidemiologic data that suggested an association between bladder cancer and AO exposure1.
  - Higher levels of exposure are associated with an approximately 2-fold increase in death from bladder cancer.
  - Currently there is limited data to explain this observation.
  - We sought to better characterize our cohort of Vietnam-era veterans with AO exposure and bladder cancer.

Methods

- Vietnam-era veterans who had been diagnosed and/or treated for urothelial carcinoma of the bladder (UCB) at the Minneapolis VA Medical Center were identified.
- Medical charts were reviewed to examine:
  - Pathologic stage and grade at diagnosis
  - Recurrence
  - Disease progression
  - Cystectomy
  - Death from disease.
- Agent Orange exposure was determined by VA registration data.
- Patients who left the VA prior to death were censored at date of last cystoscopy; those with muscle-invasion or metastasis were followed beyond this point only to determine if death occurred from UCB.

Results

- 258 patients who met inclusion criteria were identified.
- 211 patients with follow-up 12 months or greater for evaluation of recurrence and progression.
- Pathologic stage and grade at diagnosis:
  - Ta: 163 (63%)
  - Tis: 20 (8%)
  - T1: 52 (20%)
  - T2: 23 (9%)
- Pathologic grade:
  - High grade: 146 (57%)
  - Low grade: 112 (43%)
- Recurrence: 130 (62%)
- Disease progression: 36 (17%)
- Cystectomy: 25 (10%)
- Death from disease: 25 (9.7%)

Agent Orange exposure was associated with high-grade disease at presentation (controlling for age and smoking status): OR 2.13 (95% CI 1.264, 3.572, p=0.004).

Conclusions

- In our cohort of Vietnam-era veterans with UCB, AO exposure was associated with an approximately 2-fold increased risk of high grade disease at presentation.
- Further evaluation in larger cohorts is needed to better understand the mechanism leading to the increased mortality seen in epidemiologic studies.